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a degenerate helix, such as a straight line or a circle. Notice that a helix accounts rather naturally for the long repeat distance of the structure, as this would correspond to one turn of the helix. This restriction — that the phosphate-sugar groups are spacially uniform — is a great help in model building as it reduces very considerably the number of possibilities that have to be explored. Indeed at first we were unable to build any satisfactory model consistent with our assumptions, but eventually we arrived at a structure which we now belefive to be correct in its broad outlines.

This particular model does not contain just one DNA chain, but a pair of them, wound round a common axis. two chains are linked together by their bases. A base on one chain is joined by weak ph_ysical bonds to a base at the same level on the other chain, and all the bases are paired of in this way right along the structure. This is shown diagrammatically in Fig. . The general appearance of the structure is shown in a symbolic manner in Fig. , in which the two ribbons represent the phosphate sugar chains, and the pairs of bases holding them together are symbolized as horizontal rods. It will be found that this figure looks exactly the same upside down, and to preserve this feature we have built our model so that the actual sequence of atoms in one ph_osphate-sugar chain is in the opposite direction to the corresponding sequence in the other. This is shown

symbolically by the two small arrows.

Now it is found that one cannot build this model with any bases one pleases; only wertain pairs of the four bases will fit into the structure. In any pair there must always be one big one (purine) and one little one(pyrimidine). If one tries to put in two purines — two big ones, that is, — there is not sufficient room for them. Conversely a pair made of two pyrimidines is too small to bridge the gap between the two chains. Moreover when one examines in detail how the hydrogen bonds are formed between the bases it is found that (making certain plausible assumptions) the pairing is even more restricted. The only possible pairs that will fit in are

Adenine with Thymine and Guanine with Cytosine.

The way these pairs are formed is shown in Fig. .

The dotted lines show the weak physical bonds, known as hydrogen bonds, which hold the two bases of a pair together. (hydrogen bonds are, for example, the main forces holding different water molecules together, and it is because of them that water is a liquid at room temperatures and not a gas)

these specific pairs can be built into the structure either way round. We can have adanine on the first chain paired with thymine on the second, or vica versa. But if we do have adenine at some point on one of the chains, it is

essential to have thymine paired with it on the other. It is impossible to fit in guanine or cytosine or a second adenine. In the same way guanine must always be paired with cytosine.

On the other hand the model places no restriction on the sequence of pairs of bases as one proceeds along the structure. Any p specific pair can follow any other specific pair. This is because a pair of bases is flat, and as in this model they are stacked one above another like a pile of coins it does not matter which pair goes above which.

This specific pairing of the bases is the direct result of the assumption that both phosphate-sugar chains are helical. This implies that the distance apart of two sugar groups at the same level (one belonging to each chain) is always the same, no matter where one is along the chain. It follows that the bases, which are of course linked to the sugars, have always the same amount of space in which to fit, as can be seen from studying Fig. . If it were not for this restriction the bases cound hy drogen-bond together in many different ways. It is the regularity of the phosphate-sugar chains, therefore, which is at the root of the specific pairing.

Evidence for the model

The experimental evidence in support of a model of this general type is now considerable. Measurements of the density, and water content of the DNA fibres, taken with the evidence showing how the fibres can be extended in length, strongly

suggest that there are two DNA chains in the structural unit. The X-ray patterns have a large number of places where the diffraction intensity is zero and these occur exactly where one expects them from helical structures of this type. Moreover the X-ray diffraction data approximates quite closely to cylindrical symmetry, as it should. Recently Wilkins and has co-workers have given a brilliant analysis of the details of the X-ray pattern of the crystalline form, and have shown that they are consistent with a structure of this type, though in this form the bases are not perpendicular to the fibre axis, but tilted away from it.

As a the structure is a relatively stiff one it easily explains the extended shape of the BNA in solution. It is This has irreversible also consistent with the titration curve. features which suggest that the bases are hydrogen-bonded together. However the most striking support for the specific pairing of the bases comes from the recent analytical data. These show that for every species so far examined - and there are over fourty of them xxxfxx - the number of adenines in some given DNA is closely equal to the number of thymines, and the number of guanines equal to the number of cytosines, although the cross-ratio (between say adenine and guanine) can vary considerably from species to species. This remakable fact, which is exactly what one would expect from a model containing only the specific pairs, was first pointed out by Indeed, since the sequence of bases along a Dr. Chargaff.

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single chain is believed to be irregular this result is very difficult to explain except by specific pairing.

It might be thought that while this model might be correct for the DNA extracted from the cell and made into fibres the DNA in the cell was in a radically different form. This seems unlikely since it is difficult to see how the very charactaristic features of the model could be produced merely by the extraction procedure. However Dr. Wilkins has shown that it is possible to get very similar X-ray pictures from intact biological material, such as sperm heads and bacteriophage, so that there seems little doubt that the structure is biologically significant.

The present position is therefore that while the details of the structure remain to be worked out - and until this is done the model cannot be considered as proved - it seems very probable that the following statements will stand the test of time:

- 1. The structure consists of two chains
- 2. The chains are helical and wound round a common axis.
- 3. They are held together by hydrogen bonds between specific pairs of bases.
- 4. The structure occurs in biologically intact material.

A possible replication mechanism

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Now the exciting thing about a model of this type is that it immediately suggests how the DNA might produce an exact copy of itself. This is begause the model consists of two parts, each of which is the complement of the other. The basic idea is that the two chains in the structure unwind and separate. Each chain then acts as a sort of mould onto which a new complementary chain can be synthesised. When this process is complete there will be two pairs of chains where we only had one before. Moreover, because of the specific pairing of the bases the sequence of the pairs of bases will have been duplicated exactly.

As an analogy consider two photographic films, one a positive and the other a negative of the same scene. Now if

one gives the positive to one person, and asks him to print a negative from it, and also gives the original negative to another person, and ask him to print a positive from it they will end up with two pairs of photographs, each like the original pair. We shall, in effect have made an exact copy of our original pair in one step.

To see how this works out in the case of DNA let us consider the process in rather more detail. Since we have to synthesise two new chains we may require some new material. The exact precursors of DNA are not known, but let us assume for simplicity that it is built up from nucleotides, which is the name given to the small molecules which contain one phosphate, one sugar and one base.

Imagine, then, that we have a <u>single</u> helical chain of DNA, and that floating around it, inside the cell, there is a supply of the four sorts of nucleotides. Every now and then a lose nucleotide will attach itself by its base to one of the bases of the DNA chain. Now if this happens to two adjoining bases, and if the loose nucleotides are the type which can form specific pairs with those already there, they will be in just the right position to be joined together, and, eventually, to form part of the new chain. If one or both of them is <u>not</u> the correct type to go in at that point it will be impossible to join them together and before long they will diffuse elsewhere. Thus only the nucleotides with the

with the proper bases will get joined together to form the new chain.

While this process is going on the other single chain of the original pair will also be forming, in a similar manner, a new chain complementary to itself. The whole process is illustrated in figure . In Fig. was a there is shown a small stretch of the original pair of chains. In Fig. they have separated. In the next figure new chains are being formed from loose nucleotides, and in Fig. the process is complete, and it can be seen that the original pair has now been duplicated.

At the moment this idea must be regarded simply as a working hypothesis. Straight away it raises a number of questions. How do the two chains unwind? What holds a single chain in a helical configuration? (Watson and I suspect that the replication starts almost as soon as the unwinding, so that only a very short stretch is ever in the 'single' state at one time). Most important of all, how does the DNA influence the rest of the cell? We believe that the sequence of the bases along the DNA is the code that carries the genetical information, but how does it produce its effect? We can see how the code may be copied, but as yet we cannot read it.

In favour of the idea one can only say that it seems rather an odd coincidence to find in the one material which is most closely associated with replication a structure of

exactly the type one would need to carry out a specific replication xxxxxx process, namely one showing both variety and complementarity. We can only hope that the simplicity of the idea will stimulate someone to devise some new experiments which will either prove or disprove it.